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CASE REPORT

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The Sole Initial Imaging Finding in Creutzfeldt-Jacob Disease: Focal FDG-PET Hypometabolism

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ABSTRACT

Laboratory studies such as electroencephalography, cerebrospinal fluid examination and diffusion-weighted magnetic resonance imaging (DWI-MRI) are valuable in the diagnosis of Creutzfeldt-Jacob disease (CJD), . However, these laboratory studies may not show the characteristic findings in the very early stage of the disease. Here, we present a case of CJD who had atypical neurologic presentation initially and had only a focal parietal 2-(18F) fluorodeoxyglucose (FDG) positron emission tomography (PET) hypometabolism as the sole imaging abnormality at the beginning. The patient progressed rapidly, and showed typical neurological findings for CJD. The brain MRI was performed two weeks after the FDG-PET study, finally demonstrated increased signal intensity in DWI in caudat nucleus, putamen, and cerebral cortex, especially on left parietal region.

Imaging methods demonstrating functional alterations in the brain should be obtained in the early period in patients with normal MRI suspected having CJD. Repeating DWI could also be an effective diagnostic approach.

Keywords: Creutzfeldt-Jacob, positron emission tomography, PET, prion, magnetic resonance imaging

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INTRODUCTION

Creutzfeldt-Jakob disease (CJD), an untreatable cause of rapidly progressive dementia, occurs as a result of accumulation of an abnormal form of the human prion protein PrPSc in the brain. Most of the cases are sporadic but genetic, infectious, and iatrogenic forms also exist. Laboratory studies such as electroencephalography (EEG), detection of 14-3-3 protein in the cerebrospinal fluid (CSF) and magnetic resonance imaging (MRI) are valuable in the diagnosis of CJD. Among these studies typical abnormality on diffusion weighted imaging (DWI) is highly sensitive and specific in the diagnosis of CJD (1, 2). The diagnosis of early cases could be difficult, since the initial symptoms and signs are not specific, and the laboratory studies may not be a diagnostic aid in this stage. Herein, we present a case with CJD who had atypical neurological presentation with normal MRI.

CASE REPORT

A 74-year-old male patient was admitted to our hospital with six-week history of progressive weakness on the right arm, and a one-week history of dystonic posturing of the right hand and gait ataxia. His past medical history was remarkable for coronary artery disease, hyperlipidemia, and hyperthyroidism. On physical and neurological examination, he was alert and cognitively normal, had 3-/5 monoparesia on the right upper extremity and dystonic posturing of the right hand, increased deep tendon reflexes on the right side of the body, and positive Babinski sign on the right. Dysmetria on the right and gait ataxia were also evident. At this stage brain MR imaging including diffusion weighted imaging was normal (Figure 1). Laboratory studies including complete blood count, biochemistry, FT3 and FT4 were all within normal limits. TSH (0.005) was suppressed. Anti-TPO, Anti-thyroglobulin, TSH-receptor antibodies were negative. The CSF examination disclosed slightly elevated protein level (53 mg/dL) but normal glucose content. Infectious markers including syphilis serology, human immunodeficiency virus serology were all negative. Whole body positron emission tomography (PET), paraneoplastic markers (Anti-hu, anti-yo, Anti-ri, PCA1–2-tr, Amphyphysin, CRMP 5 IgG, P/Q type calcium channel Ab, N type calcium channel Ab, Ach receptor binding Ab) and tumor markers (free PSA, PSA, CEA, Ca19.9, AFP, B2-microglobulin) were studied to exclude paraneoplastic etiologies. All of the markers were negative, and chest computerized tomography (CT) and abdominal ultrasonography were normal. Body fluorodeoxyglucose (FDG) PET imaging was normal but brain imaging displayed decreased cerebral metabolic rate for glucose of left posterior parietal region (Figure 2a). In two weeks, he rapidly deteriorated, and developed cerebellar and pyramidal signs on the left and his speech became dysarthric. He was unable to walk without aid. Cognition was slowed. A repeat brain MRI did not disclose any abnormality. Motor evoked potential (MEP) study showed elongation of central motor conduction time and a somatosensory evoked potential (SEP) study demonstrated increased

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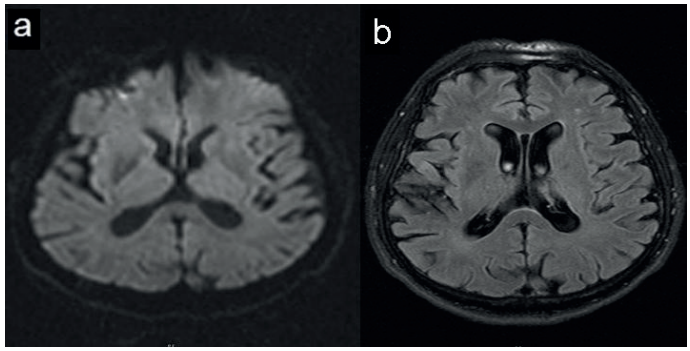

Figure 1. Axial diffusion (a) and FLAIR (b) sequences of the brain MRI does not show any signal changes supporting CJD.

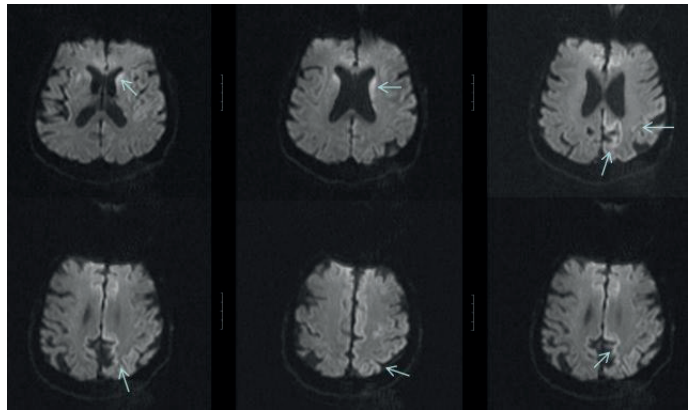

Figure 3. DWI performed two weeks after FDG-PET shows increased signal intensity in caudat nucleus, putamen and cortical regions (arrows).

latency of cortical potentials on the left implying the presence of cerebral pathology. He continued to deteriorate, and became bedridden. A remarkable cognitive decline and stimuli induced myoclonus developed. EEG was performed and demonstrated presence of pseudoperiodic, 1–2 Hz sharp wave activities which were suggestive for CJD. Third brain MRI performed two weeks after the FDG-PET study finally demonstrated increased signal intensity in caudat nucleus, putamen, and cerebral cortex, especially on left parietal region on the DWI (Figure 2b). Repeat CSF examination demonstrated elevated 14-3-3 protein. He was finally diagnosed as probable sporadic CJD (sCJD). Because we decided to report our experience with a single case the informed consent was obtained from the relatives of the patient.

DISCUSSION

The clinical findings, CSF analysis and MRI results of our patient were compatible with the probable sCJD. In addition, normal MRI with atypical neurological findings was a challenging condition at the beginning. Hence, other possible causes including paraneoplastic encephalitis, Hashimoto encephalopathy and corticobasal degeneration in differential diagnosis were excluded. Although the presenting clinical feature was not specific for the disease, he rapidly developed ataxia, myoclonus, and cognitive disturbance that made clinical picture more typical to CJD. The definite diagnosis of sCJD can only be possible pathologically but the diagnosis of living patients is also possible with considerable high sensitivity and specificity when positive laboratory findings are obtained. Demonstration of focal cortical hypometabolism in FDG-PET imaging even before the appearance of DWI abnormality presents the interesting feature of this patient.

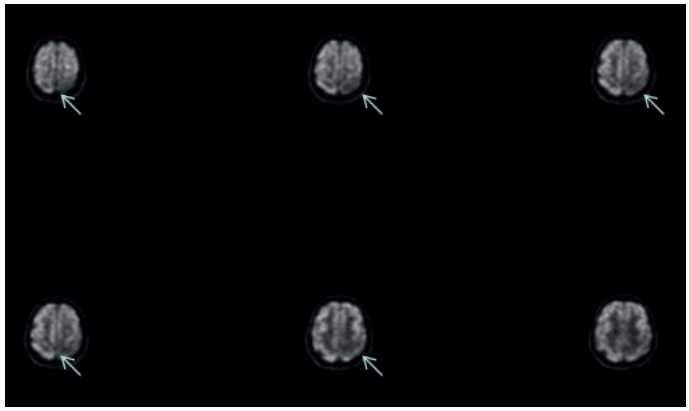

Figure 2. FDG-PET, brain images demonstrates decreased cerebral metabolic rate for glucose of left posterior parietal region (arrows).

The most suggestive radiologic pattern for CJD is the extensive cortical gray matter hyperintensities and additional striatal abnormality on both FLAIR and DWI images (2). The pattern of FLAIR/DWI hyperintensity and restricted diffusion can differentiate sCJD from other rapid progressive dementias with a high sensitivity and specificity (3). Serial MRI studies disclosed that mild atrophic changes could be the only abnormality in early cases, and subsequently increased signal intensity in basal ganglia and cortex become evident on DWI, FLAIR, or T2-weighted images (4). Several CJD cases studied with brain FDG-PET or single-photon emission computed tomography (SPECT) were also reported. These studies implied that FDG-PET or SPECT may detect functional cerebral abnormality even before the appearance of morphologic abnormality in the structural brain images (5–8). Focal, asymmetrical or widespread hypometabolism may be seen in CJD probably reflecting the stage of the disease (5, 9). In cases that were studied with both FDG-PET and DWI-MRI, regions of hypometabolism detected by FDG-PET usually correspond to high signal regions observed on DWI images (10). Analysis of FDG-PET images showed that pathological findings are extended to more cortical and subcortical areas than specific DWI-MRI findings (8). It has also shown that PET-CT imaging is able to detect abnormalities in the basal ganglia and thalamus without corresponding DWI hyperintensities (7, 11). CJD patients exhibit a characteristic pattern of hypometabolism in the basal ganglia and/or thalamus with mainly frontal extensive cortical affection while Fatal Familial Insomnia (FFI) is characterized by thalamic hypometabolism on PET-CT (8). In one case report of thalamic variant of familial CJD, it is clearly stated that unilateral thalamic hypoperfusion was identified with SPECT before the emergence of increased signal intensity in DWI images (12). It was stated that cortical hypometabolism on PET-CT is bilateral in most patients mainly including frontal and temporal cortex. and less frequently parietal or occipital areas (8). It is also interesting that our patient showed unilateral hypometabolism at the early stage in an infrequent area: the parietal lobe. It is also mentioned that FDG-PET is more sensitive than MRI for the cortex while it has less sensitivity compared to MRI in subcortical areas (13).

CONCLUSION

The present case clearly demonstrates that although the sensitivity of DWI approaching to 100% was reported in CJD, DWI signal changes can be a late event (14). Other imaging methods demonstrating functional alterations in the brain should be obtained in the early period in patients with normal MRI suspected having CJD. FDG-PET could be valuable to distinguish CJD from other rapid progressive dementias.

Ethics Committee Approval: This study was carried out in accordance with the Helsinki Declaration.

Informed Consent: Informed constend was obtained.

Peer-review: Externally peer-reviewed.

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